

CLAIMS

1. An isolated nucleic acid molecule, comprising
- (a) nucleic acid molecules which hybridize under stringent conditions to a molecule consisting of a nucleic acid of SEQ ID NO:1 and which code for a Lens Epithelial Cell Derived Growth Factor polypeptide,
- (b) deletions, additions and substitutions of (a) which code for a respective lens epithelial cell derived growth factor polypeptide,
- (c) nucleic acid molecules that differ from the nucleic acid molecules of (a) or (b) in codon sequence due to the degeneracy of the genetic code, and
- (d) complements of (a), (b) or (c).
2. The isolated nucleic acid molecule of claim 1; wherein the isolated nucleic acid molecule comprises SEQ ID NO:1.
3. The isolated nucleic acid molecule of claim 1, wherein the isolated nucleic acid molecule is the nucleic acid molecule of SEQ ID NO:13 or a fragment thereof.
4. An isolated nucleic acid molecule selected from the group consisting of
- (a) a fragment of a nucleic acid molecule of SEQ ID NO:1, of sufficient length to represent a sequence unique within the human genome, and identifying a nucleic acid encoding a Lens Epithelial Cell Derived Growth Factor polypeptide,
- (b) complements of (a),
- provided that the fragment includes a sequence of contiguous nucleotides which is not identical to any sequence selected from the sequence group consisting of
- (1) sequences having the GenBank accession numbers of Table III,
- (2) complements of (1), and
- (3) fragments of (1) and (2).
5. The isolated nucleic acid molecule of claim 4, wherein the sequence of contiguous nucleotides is selected from the group consisting of:
- (1) at least two contiguous nucleotides nonidentical to the sequence group,
- (2) at least three contiguous nucleotides nonidentical to the sequence group,

- (3) at least four contiguous nucleotides nonidentical to the sequence group,
- (4) at least five contiguous nucleotides nonidentical to the sequence group,
- (5) at least six contiguous nucleotides nonidentical to the sequence group,
- (6) at least seven contiguous nucleotides nonidentical to the sequence group.

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6. The isolated nucleic acid molecule of claim 4, wherein the fragment has a size selected from the group consisting of at least: 8 nucleotides, 10 nucleotides, 12 nucleotides, 14 nucleotides, 16 nucleotides, 18 nucleotides, 20, nucleotides, 22 nucleotides, 24 nucleotides, 26 nucleotides, 28 nucleotides, 30 nucleotides, 50 nucleotides, 75 nucleotides, 100 nucleotides, and 200 nucleotides.

7. The isolated nucleic acid molecule of claim 4, wherein the molecule encodes a polypeptide, or a fragment of, which binds a human antibody.

8. An expression vector comprising the isolated nucleic acid molecule of claims 1, 2, 3, 4, 5, 6, or 7 operably linked to a promoter.

9. An expression vector comprising the isolated nucleic acid molecule of claim 4 operably linked to a promoter.

10. A host cell transformed or transfected with the expression vector of claim 8.

11. A host cell transformed or transfected with the expression vector of claim 9.

12. An isolated polypeptide encoded by the isolated nucleic acid molecule of claim 1, 2, or 3, wherein the polypeptide, or fragment of the polypeptide, has protein synthesis induction activity.

13. The isolated polypeptide of claim 12, wherein the isolated polypeptide is a secreted protein encoded by the isolated nucleic acid molecule of claim 2.

14. The isolated polypeptide of claim 13, wherein the isolated polypeptide comprises a

polypeptide having the sequence of amino acids 1-530 of SEQ ID NO:2.

15. An isolated polypeptide encoded by the isolated nucleic acid molecule of claim 1, 2, or 3, wherein the polypeptide, or fragment of the polypeptide, is immunogenic.

16. The fragment of claim 15, wherein the fragment, or portion of the fragment, binds a human antibody.

17. An isolated polypeptide which binds selectively a polypeptide encoded by the isolated nucleic acid molecule of claim 1, 2 or 3.

18. The isolated polypeptide of claim 17, wherein the isolated polypeptide binds to a polypeptide having the sequence of amino acids of SEQ ID NO:2.

19. The isolated polypeptide of claim 17, wherein the isolated polypeptide binds to a polypeptide selected from the group consisting of a polypeptide having the sequence of amino acids of SEQ ID NO:4, a polypeptide having the sequence of amino acids of SEQ ID NO:6, and a polypeptide having the sequence of amino acids of SEQ ID NO:8.

20. The isolated polypeptide of claim 17, wherein the isolated polypeptide binds to a polypeptide having the sequence of amino acids of SEQ ID NO:2.

21. The isolated polypeptide of claim 20, wherein the isolated polypeptide is an antibody or an antibody fragment selected from the group consisting of a Fab fragment, a F(ab)₂ fragment or a fragment including a CDR3 region selective for the polypeptide having the sequence of amino acids of SEQ ID NO:2.

22. An isolated polypeptide comprising a fragment of the polypeptide of claim 12 of sufficient length to represent a sequence unique within the human genome and identifying a polypeptide that has protein synthesis induction activity, provided that the fragment includes a sequence of contiguous amino acids which is not identical to any sequence selected from the sequence group consisting of SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID

NO:12, and SEQ ID NO:22.

23. A method for determining an individual's susceptibility to developing cataracts, comprising:

5 a) obtaining a test sample from the individual containing antibodies,
 b) measuring the level of anti-LEDGF antibodies in the test sample,
 c) comparing the level of anti-LEDGF antibodies in the test sample to a control,
wherein the level of anti-LEDGF antibodies compared to the control is indicative of the individual's susceptibility to developing cataracts.

10 24. The method of claim 23, wherein the test sample is blood.

 25. The method of claim 23, wherein the test sample is tissue selected from the group consisting of epidermis and buccal scrapings.

 26. A kit, comprising a package containing:

 an agent that selectively binds to the isolated nucleic acid of claim 1 or an expression product thereof, and

 a control for comparing to a measured value of binding of said agent to said isolated nucleic acid of claim 1 or expression product thereof.

20 27. The kit of claim 26, wherein the control is a predetermined value for comparing to the measured value.

25 28. The kit of claim 26, wherein the control comprises an epitope of the expression product of the nucleic acid of claim 1.

 29. A kit, comprising a package containing:

 an epitope that selectively binds to an anti-LEDGF antibody, and

30 a control for comparing to a measured value of binding of said epitope to said anti-LEDGF antibody.

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30. The kit of claim 29, wherein the epitope is SEQ ID NO:2 or an anti-LEDGF antibody binding fragment thereof, and wherein said control is a predetermined value.

31. A method for treating a subject with an elevated level of anti-LEDGF antibodies to inhibit the development of cataracts, comprising:

administering to a subject in need of such treatment a polypeptide of claim 12 in an amount effective to suppress the level of anti-LEDGF antibodies in the subject, thereby inhibiting the formation of opacities in a crystalline lens of the subject.

32. The method of claim 31, wherein the polypeptide of claim 12 is administered orally.

33. The method of claim 31, wherein the polypeptide of claim 12 is administered intravenously.

34. The method of claim 31, wherein the polypeptide of claim 12 is administered through a nasal spray.

35. A method for determining the level of LEDGF expression in a subject, comprising:

- a) obtaining a test sample from the individual,
- b) measuring the expression of LEDGF in the test sample,
- c) comparing the measured expression of LEDGF to a control.

36. The method of claim 35, wherein the expression of LEDGF in (b) is LEDGF mRNA expression.

37. The method of claim 35, wherein the expression of LEDGF in (b) is LEDGF polypeptide expression.

38. The method of claim 35, wherein the test sample is tissue.

39. The method of claim 35, wherein the test sample is a biological fluid.

40. The method of claim 36, wherein LEDGF mRNA expression is measured using the Polymerase Chain Reaction (PCR).

41. The method of claim 36, wherein LEDGF mRNA expression is measured using northern blotting.

42. The method of claim 37, wherein LEDGF polypeptide expression is measured using monoclonal antisera to LEDGF.

43. The method of claim 37, wherein LEDGF polypeptide expression is characterized using polyclonal antisera to LEDGF.

44. A method for treating a subject with a cancer expressing LEDGF, comprising:
administering to a subject in need of such treatment an agent that selectively binds to an isolated nucleic acid molecule of claim 1 or an expression product thereof, in an amount effective to decrease LEDGF activity in the cancer and inhibit the proliferation of the cancer.

45. The method of claim 44, wherein the agent is an antisense nucleic acid.

46. The method of claim 44, wherein the agent is an isolated polypeptide.

47. A pharmaceutical composition comprising:
a pharmaceutically effective amount of an agent comprising of an isolated nucleic acid molecule of claim 1 or an expression product thereof, and
a pharmaceutically acceptable carrier.

48. The pharmaceutical composition of claim 47 wherein the agent is an expression product of the isolated nucleic acid molecule of claim 1.

49. A method for decreasing LEDGF mediated activity in a subject, comprising:
administering to a subject in need of such treatment an agent that selectively binds to an isolated nucleic acid molecule of claim 1 or an expression product thereof, in an amount

effective to decrease LEDGF mediated activity in the subject.

50. The method of claim 49, wherein the agent is an antisense nucleic acid.

5 51. The method of claim 49, wherein the agent is an isolated polypeptide.

52. A method for inducing cell-death in a cell, comprising:

contacting the cell with an agent that selectively binds to an isolated nucleic acid molecule of claim 1 or an expression product thereof, in an amount effective to decrease LEDGF mediated activity in the cell and to induce cell-death .

53. The method of claim 52, wherein the agent is an antisense nucleic acid.

54. The method of claim 52, wherein the agent is an isolated polypeptide.

55. A method for inhibiting differentiation of a cell *in vitro*, comprising:

contacting a cell *in vitro* with an agent that selectively binds to an isolated nucleic acid molecule of claim 1 or an expression product thereof, in an amount effective to decrease LEDGF mediated activity in the cell and inhibit differentiation of the cell.

56. The method of claim 55, wherein the agent is an antisense nucleic acid.

57. The method of claim 55, wherein the agent is an isolated polypeptide.

25 58. A method for increasing cell proliferation, comprising:

contacting a cell expressing a LEDGF receptor with an agent that increases LEDGF stimulated cell proliferation in an amount effective to stimulate cell proliferation.

59. The method of claim 58, wherein the agent is a polypeptide encoded by the nucleic acid of SEQ ID NO:1.

60. The method of claim 58, wherein the agent is a polypeptide having the amino acid

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sequence of SEQ ID NO:2, or a LEDGF receptor stimulatory fragment thereof.

61. A method for promoting wound healing in a subject, comprising:
administering to a subject in need of such treatment an agent that increases LEDGF stimulated
cell proliferation, in an amount effective to promote wound healing in the subject.

62. The method of claim 61, wherein the agent is a polypeptide encoded by the nucleic
acid of SEQ ID NO:1.

63. The method of claim 61, wherein the agent is a polypeptide having the amino acid
sequence of SEQ ID NO:2, or a LEDGF receptor stimulatory fragment thereof.

64. A method for inhibiting environmental stress-induced cell-death, comprising:
contacting a cell expressing a LEDGF receptor, under environmental stress
otherwise sufficient to induce cell-death, with an agent that increases LEDGF mediated
activity in an amount sufficient to inhibit death of said cell which otherwise would result from
said environmental stress.

65. The method of claim 64, wherein the cell contacted forms part of a tissue.

66. The method of claim 64, wherein the cell contact occurs *in vitro*.

67. The method of claim 64, wherein the environmental stress is selected from the group
consisting of: physical trauma, oxidative stress, chemical stress, and UV irradiation.

68. The method of claim 64, wherein the agent is a polypeptide encoded by the nucleic
acid of SEQ ID NO:1.

69. The method of claim 64, wherein the agent is a polypeptide having the amino acid
sequence of SEQ ID NO:2, or an LEDGF receptor stimulatory fragment thereof.

70. A method for increasing heat-shock protein activity in a cell, comprising:

contacting the cell with an isolated nucleic acid molecule of claim 1 or an expression product thereof, in an amount effective to increase LEDGF mediated activity in the cell and to increase heat-shock protein activity in the cell.

5 71. The method of claim 70, wherein the cell contacted forms part of a tissue.

72. The method of claim 70, wherein the cell contact occurs *in vitro*.

73. The method of claim 70, wherein the expression product is a polypeptide encoded by
10 the nucleic acid of SEQ ID NO:1.

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